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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/558,232
Filing Date: April 26, 2000
Appellant(s): MANYAK ET AL.

Donald R. McKenna (Reg. No. 44,922)
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 01, 2008 appealing from the Office action mailed March 07, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Weinstein et al., Science, Vol. 275, pages 343-349, 1997.

Antman et al., JAMA, Volume 268, pages 240-248, 1992.

Ogata et al., Nucleic Acids Research, Volume 27, Pages 29-34, 1999.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

CLAIM REJECTIONS - 35 USC § 103

1. Claims 1-3, 10, 14-23, 27, 28, 33-43, 59-64, 67, 68, 70-76, 78-105, 107, 108, 110, 120, 121, 124-129, 132, 139-142, 144, and 145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinstein et al. (1997) (Weinstein hereafter) taken with Antman et al. (1992) (Antman hereafter).

MOTIVATION TO COMBINE

2. Antman et al. discloses an improvement for "better databases" for the treatment of patients in clinical trials (page 240, Conclusions §). While, Weinstein describes a method of selecting compounds clinical trials (page 344, column 1, lines 10-16) and providing clinical databases (page 348, column 2, lines 22-23). An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by Antman et al. to modify the clinical database of Weinstein for better databases for the treatment of patients in clinical trials.

BASIS OF REJECTION

3. In regard to claims 1, 17, 33, 35, 37-40, 59-61, 63, 64, 132, 139, and 142, Weinstein describes a computer system comprising:

a. A first database containing, records corresponding to a plurality of chemical compounds and records corresponding to biological information related to effects

of such chemical compounds on biological systems (page 344, column 2, line 4, to column 3, lines 4-22, especially, "chemical structure (S) database");

b. A second database containing records corresponding to a plurality of molecular targets (page 344, column 2, line 23, to column 3, line 22, especially, "target (T) database", and Figure 1, Database T);

c. A third database containing records corresponding to results from *in vitro* assays measuring interactions between each of a plurality of compounds in the first database and each of a plurality of molecular targets in the second database, the results including information on the effect that a compound selected from the first database has on the interaction between a reference compound know to interact with a selected molecular target from the second database and said selected molecular target (page 343, column 3, last paragraph, e.g. inhibitors, and page 344, Figure 1, especially, the text description of Database A); and

d. A user interface allowing a user to provide the system with information about a new chemical compound (page 343, column 3, last paragraph, especially, ""Given one compound as a 'seed'…", and page 344, column 1, lines 25-33, especially, "Portions of these databases can been accessed through DTP's World Wide Web site"); and

e. A query script that extracts information from the three databases that is relevant to the predictability of the potential use of the new compound as a drug (page 349, column 1, item 21, "especially, "DISCOVERY uses…scripting…").

4. However, Weinstein does not disclose the limitation of a first database of chemical compounds that have failed in preclinical or human clinical tests, as in instant claims 17 and 142, and as an option of the elected subject matter species.

5. Antman describes literature a search for meta-analyses and randomized control trials using the Medline database (page 241, column 2, last paragraph). The searches resulted in data directed to treatments that have no effect on mortality or are potentially harmful (page 240, Data Synthesis §) and "negative trial, suggesting that the treatment does not work" (failed in human clinical tests) (page 246, column 1, "Negative" RCTs §). Therefore, it would have been obvious to one of ordinary skill in the art to modify the clinical databases of Weinstein with information about "negative trial, suggesting that the treatment does not work" (failed in human clinical tests) as described by Antman for better databases for the treatment of patients in clinical trials.

6. In regard to claim 2, Weinstein describes the interaction includes binding and the effect includes inhibitory effect (page 343, column 2, lines 4-8, especially, "the NCI established a primary screen in which compounds are tested in vitro for their ability to inhibit…").

7. In regard to claims 3, 27, 41, 42, 103, and 125, Weinstein describes the chemical compounds includes compounds with known biological activity such as binding (page 343, column 2, lines 4-8, especially, "the NCI established a primary screen in which compounds are tested in vitro for their ability to inhibit…").

8. In regard to claim 10, 67, 68, 108, and 110, Weinstein describes the molecular targets include receptors (page 344, column 2, line 35, especially, "cytokine receptors").

9. In regard to claims 14, 15, 18, 19, and 22, Weinstein describes the records of the first database corresponding to a plurality of chemical compounds are organized in categories related to the description and properties of the compounds (page 344, column 2, line 4, to column 3, lines 4-22, especially, "chemical structure (S) database").

10. In regard to claim 16, Weinstein describes the first database includes a natural product database (page 343, column 3, lines 5-7, and page 348, column 3, item 10, especially, "synthetic compounds and for natural product extracts").

11. In regard to claim 20, Weinstein describes the second database includes a sequence/mutation database (page 345, Figure 2, especially, the description of the figure "p53 seq, p53 sequence, wild-type versus mutant").

12. In regard to claim 21, Weinstein describes the second database includes a genomic database (page 348, column 2, "the plasticity of a poorly controlled genome…").

13. In regard to claim 23, Weinstein describe means for setting an interaction test threshold corresponding to said effect and means for selecting the compound when its results in a test meeting the interaction threshold (page 344, column 1, lines 10-16, especially, "five compounds…assessed in the screen and analyzed…selected for entry into clinical trials").

14. In regard to claims 28, 34, 36, 43, and 99, Weinstein describes the chemical compounds include compounds with known biological activity (page 344, column 2, line 4, to column 3, lines 4-22, especially, "chemical structure (S) database").

15. In regard to claim 62, Weinstein describes a fourth database containing records corresponding to the effect of chemical compounds contained in the first database on biological systems (page 344, Figure 1, especially, the text description of Database A).

16. In regard to claims 70 and 76, Weinstein describes the third database contains records corresponding to complete sets of results from a screening process ("the NCI established a primary screen in which compounds are tested in vitro for their ability to inhibit…").

17. In regard to claims 71-75 and 80, Weinstein describes records in the third database corresponding to the results of tests to determine the interaction between compounds in the first database and targets in the second database includes positive interactions and negative or lack of interactions (page 346, column 3, lines 11-12, especially, "highly negative", and page 347, column 1, lines 7-8, "correlate positively").

18. In regard to claims 78, 128, and 129, Weinstein describes the tests used to generate results comprising the third database are based on reporter gene assays or functional assays (page 343, column 2, lines 4-8, especially, "the NCI established a primary screen in which compounds are tested in vitro for their ability to inhibit growth of 60 different human cell lines", and page 346, column 3, lines 16-20, especially, "transport assays").

19. In regard to claims 79 and 81-86, Weinstein describes the limitation of determine interaction as numerical values (page 345, Figure 2, description of figure, especially, "high positive Pearson correlation coefficient…selective potency against cells that have less target or function", and page 346, Figure 4, especially, "Wilcoxon P value").

20. In regard to claims 87, 88, 95, 144, and 145, the limitations of LOPAC, United States Pharmacopeial Convention Inc.'s USP DI Series, and SMILES codes are directed to nonfunctional descriptive material. The limitations are directed to compilation of facts or data merely stored to be read without creating any functional interrelationship with the claimed subject matter. The MPEP states that when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in terms of patentability. For example, the claimed computer system differs from the prior art solely with respect to the limitation of LOPAC, United States Pharmacopeial Convention Inc.'s USP DI Series, or SMILES codes, nonfunctional descriptive material, that cannot alter how the machine functions (i.e., the descriptive material does not reconfigure the computer). See MPEP 2106, §VI. Therefore, the cited disclosure of Weinstein and Antman renders the claims obvious over the prior art.

21. In regard to claims 89-94, Weinstein describes records corresponding to the chemical compounds in the first database include at least a chemical name etc. (page 344, column 2, line 4, to column 3, lines 4-22, especially, "chemical structure (S) database"). The noted that the descriptors cited above have been reasonably interpreted as "can be analyzed using the methods of recursive partitioning" because the method of Weinstein requires the "clustered correlation" (page 345, column 3, lines 5-26).

22. In regard to claims 96-98, and 120, Weinstein describes records corresponding to the chemical compounds in the first database include 3-D pharmacophore (page 344, column 2, line 4, to column 3, lines 4-22, especially, "chemical structure (S) database").

23. In regard to claims 100-102, 140, and 141, Weinstein describes the records in the first database corresponding to biological information includes information on chemical name…toxicity etc. (page 347, column 2, "genotoxic stress").

24. In regard to claims 104 and 127, Weinstein describes records in the first database corresponding to biological information related to mechanism of action of selected chemical compounds on biological systems includes information on at least one of the following categories: major pathway (page 347, column 2, "Activity Patterns and p53 Pathway Status").

25. In regard to claims 105 and 121, Weinstein describes records corresponding to biological information related to effects of the chemical compounds on biological systems can be searched and analyzed using computer based searching and data analysis methods (page 347, column 3, last paragraph).

26. In regard to claim 107, Weinstein describes such as value as GI50 (page 343, Abstract etc.). However, Weinstein does not explicitly describe the well known in the art numerical terms such as LD50, ED50, percent absorbed, half-life, and peak concentration for compound activity. Weinstein "Each compound's pattern is like a fingerprint, essentially unique among the many billions of distinguishable possibilities (Abstract etc.). Further, patterns of activity observed in the screen have proved predictive in an even more powerful way at the molecular level (page 343, column 3, lines 18-20). Therefore, it would have been obvious for one of ordinary skill in the art to modify the method of Weinstein in view of Antman to incorporate the well known in the art activity such as LD50, ED50, percent absorbed, half-life, and peak

concentration for compound activity for more powerful way of predicting potential therapeutic agent.

27. In regard to claim 124, Weinstein describes records corresponding to the molecular targets in the second database are grouped by family, superfamily, or subfamily (page 345, Figure 2, especially, the description describing "cisplatin-carboplatin family").

28. In regard to claim 126, Weinstein describes records corresponding to the molecular targets in the second database are organized by location of expression tissues (page 343, column 2, last two lines, to column 3, line 2, especially, "cancer of breast, prostate, lung…").

29. Claims 77, 122, and 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinstein et al. (1997) (Weinstein hereafter) taken with Antman et al. (1992) (Antman hereafter) as applied to claims 1-3, 10, 14-23, 27, 28, 33-43, 59-64, 67, 68, 70-76, 78-105, 107, 108, 110, 120, 121, 124-129, 132, 139-142, 144, and 145 above, and further in view of Ogata et al. (1999) (Ogata hereafter).

MOTIVATION TO COMBINE

30. Antman et al. discloses an improvement for "better databases" for the treatment of patients in clinical trials (page 240, Conclusions §). Weinstein describes a method of selecting compounds for clinical trials (page 344, column 1, lines 10-16) and providing clinical databases (page 348, column 2, lines 22-23) based on biochemical pathways (page 348, column 1, last paragraph). Ogata describes LIGAND as being tightly integrated with KEGG (biochemical pathways) as well as with most of the major molecular biology

databases (Ogata, page 29, column 2, lines 1-6). An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by Antman et al. to modify the clinical database of Weinstein by incorporating the pathway information of Ogata for better databases for the treatment of patients in clinical trials.

BASIS FOR REJECTION

31. In regard to claim 77, Weinstein and Antman describe all the limitations of said claims, except for the limitation inositol triphosphate. Ogata describes the limitation of inositol triphosphate (page 30, Table 2). Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use KEGG as described by Weinstein, Ogata, and Antman for better databases for the treatment of patients in clinical trials.

32. In regard to claims 122 and 123, Weinstein and Antman describe all the limitations of said claims, except for the limitation of "sequence alignment" or "sequence homology." Ogata describes the sequence alignment and homology (Page 33, Column 1, Lines 33 and Figure 3, Table 3, and Page 33, Column 2, Lines 54-55). Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use KEGG as described by Weinstein, Ogata, and Antman for better databases for the treatment of patients in clinical trials.

(10) Response to Argument

On page 9, Applicant argues Weinstein reference does not disclose the use of a biological activity database in the manner specified in the claims because the claimed invention requires the use of a database that contains actual clinical data from both FDA-approved drugs and drugs that have failed clinical trials. Applicant's argument is not persuasive because Weinstein in view of Antman describes the claimed invention as discussed below. First, claim 1 recites a first database containing a plurality of compounds and records corresponding to biological information. Claim 17 recites the elected species of "the first database includes a database of chemical compounds that have failed in preclinical or human clinical tests." However, neither claim recites the argued limitation of a database that contains actual clinical data from both FDA-approved drugs and drugs that have failed clinical trials. Further, neither claim requires the first database to have any biological activity as argued by applicant. As for the limitation of a first database containing, records corresponding to a plurality of chemical compounds and records corresponding to biological information related to effects of such chemical compounds on biological systems, the cited "Database S" reasonably describes the claimed first database because "Database S" contains molecular features of the tested compounds which has been reasonably interpreted as biological information related to effects of such chemical compounds on biological systems.

On pages 9-10, Applicant argues Antman fails to disclose the type of biological activity database specified in the claims. It is noted as discussed above neither claim 1 or 17 of the elected species recites any type of biological activity database as argued by Applicant. As for the elected species of "the first database includes a database of chemical compounds that have

failed in preclinical or human clinical tests," Antman describes literature a search for meta-analyses and randomized control trials using the Medline database (page 241, column 2, last paragraph). The searches resulted in data directed to treatments that have no effect on mortality or are potentially harmful (page 240, Data Synthesis §) and "negative trial, suggesting that the treatment does not work" (failed in human clinical tests) (page 246, column 1, "Negative" RCTs §). Therefore, it would have been obvious to one of ordinary skill in the art to modify the clinical databases of Weinstein with information about "negative trial, suggesting that the treatment does not work" (failed in human clinical tests) as described by Antman for better databases for the treatment of patients in clinical trials.

On page 10, Applicant argues Antman simply does not disclose a relational database that can be queried as required in the pending claims. Applicant's arguments against the references individually is not persuasive because one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, the claims do not require the databases to be relational databases or queries as argued by Applicant.

As for the argument of the claimed invention is directed to an automated analysis which is distinct from the manual collection of Antman, Applicant's argument is not persuasive because the argued claims do not required any automation.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. the use of a biological activity database in the manner specified in the claims because the claimed invention

requires the use of a database that contains actual clinical data from both FDA-approved drugs and drugs that have failed clinical trials, and relational database) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

As for the motivation to combine the disclosure of Antman with Weinstein, Antman et al. discloses an improvement for "better databases" for the treatment of patients in clinical trials (page 240, Conclusions §). While, Weinstein describes a method of selecting compounds clinical trials (page 344, column 1, lines 10-16) and providing clinical databases (page 348, column 2, lines 22-23). An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by Antman et al. to modify the clinical database of Weinstein for better databases for the treatment of patients in clinical trials.

As for the argument that the "Weinstein reference fails to disclose the limitation of data describing the result of three compound interaction (molecular target/reference compound/candidate drug compound)...", Weinstein the results including information on the effect that a compound selected from the first database has on the interaction between a reference compound know to interact with a selected molecular target from the second database and said selected molecular target (page 343, column 3, last paragraph, e.g. inhibitors, and page 344, Figure 1, especially, the text description of Database A). Weinstein describes a list of agents predicted to be good Pgp substrates and Pgp inhibitors (page 344, column 3, last paragraph). It is well known in the art that inhibitors are a substance that reduces the activity of another substance (as an enzyme). As pointed to by Applicant, the three compound interaction is directed to

"determining whether it is effective in inhibiting the binding of a specific chemical compound…" The screening of inhibitors by Weinstein reasonably describes the argued limitation as exemplified in the instant specification.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Cheyne D Ly/

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